IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Examining Operations

Applicant(s): McIntosh et al

Serial No: Art Unit: 1644

Filed: Herewith Examiner: Tung, M.

TITLE: MESENCHYMAL STEM CELLS FOR PREVENTION AND TREATMENT OF IMMUNE RESPONSES IN TRANSPLANTATION

Docket No.: 640100-441

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Please amend the application as follows prior to examination::

In the Specification:

Please amend the specification as follows:

Please delete the paragraph on page 1, lines 8-11, and replace it with the following:

This application is a divisional of U.S. Patent Application Serial No. 09/427,333, filed 26 October 1999, which was a Continuation-in-Part of U.S. Patent Application Serial No. 09/267, 536 filed March 12, 1999, which is based on and claims priority of U.S. Provisional Application Serial No. 60/078,463, filed March 18, 1998, and U.S.

Provisional Application Serial No. 60/089,964, filed June 19, 1998, the disclosures of which are hereby incorporated by reference in their entirety.

In the Claims:

Please cancel claims 1-46 without prejudice. Please add the following new claim set:

93. (New) A process for reducing an immune response of effector cells against an alloantigen, comprising contacting effector cells with mesenchymal stem cells in an amount effective to reduce an immune response against an alloantigen whereby said effector cells upon contact with an alloantigen have a reduced immune response against said alloantigen.

94. (New) The process of claim 93 wherein said effector cells are T cells.

95. (New) The process of claim 94 wherein the T cells are from the donor and the alloantigen is from the recipient.

96. (New) The process of claim 94 wherein the T cells are from the recipient and the alloantigen is from the donor.

97. (New) The process of claim 94 wherein said T cells are present in a transplant.

98. (New) The process of claim 94 wherein said mesenchymal stem cells are administered to a transplant recipient suffering from graft-versus-host disease.

99. (New) The process of claim 94 wherein prior to said administration said mesenchymal stem cells (MSCs) have been expanded in culture.

100. (New) The process of claim 94 wherein said effector cells are T cells previously activated and said immune response is the reactivation of said T cells.

101. (New) The process of claim 94 wherein the transplant is skin.

102. (New) The process of claim 94 wherein the mesenchymal stem cells are administered to the transplant recipient to treat rejection of the transplant by the recipient.

103. (New) The process of claim 94 wherein the mesenchymal stem cells are human mesenchymal stem cells.

104. (New) The process of claim 94 further comprising administering to the recipient immunosuppressive agents.

105. (New) The process of claim 94 wherein the transplant is a solid organ.

106. (New) The process of claim 105 wherein the solid organ is selected from heart, pancreas, kidney, lung or liver.

107. (New) The process of claim 94 wherein said mesenchymal stem cells are administered prior to said transplant.

108. (New) The process of claim 94 wherein said mesenchymal stem cells are administered concurrently with said transplant.

109. (New) The process of claim 94 wherein said mesenchymal stem cells are administered as part of the transplant.

110. (New) The process of claim 94 wherein the mesenchymal stem cells are administered subsequent to transplant.

111. (New) The process of claim 94 wherein said mesenchymal stem cells are administered intravenously to the recipient.

112. (New) The process of claim 94 wherein said effector cells are cells of a recipient of said donor transplant.

113. The process of claim 93 wherein said mesenchymal stem cells are xenogeneic to the donor of the transplant.

114. The process of claim 93 wherein said mesenchymal stem cells are xenogeneic to the recipient of the transplant.

115. The process of claim 93 wherein said mesenchymal stem cells are xenogeneic to both the donor and the recipient of the transplant.

116. (New) The process of Claim 93 wherein the mesenchymal stem cells have been co-cultured with T cells undergoing a mixed lymphocyte reaction.

117. (New) A process for treating a transplant recipient for graft versus host disease, comprising treating the recipient of a donor transplant with mesenchymal stem cells in an amount effective to reduce an immune response against the recipient by the transplant.

118. (New) A process for reducing an immune response against an alloantigen, comprising contacting immune effector cells with at least one member selected from the group consisting of xenogeneic mesenchymal stem cells and a supernatant of xenogeneic mesenchymal stem cells in an amount effective to reduce the immune response.

119. (New) A composition for reducing an adverse immune response against a donor transplant, comprising a member selected from the group consisting of mesenchymal stem cells and a supernatant from a mesenchymal stem cell culture in an amount effective to inhibit or reduce an adverse immune response against a donor transplant, and a pharmaceutical carrier.

120. (New) The composition of claim 119 wherein the mesenchymal stem cells are autologous to the recipient.

121. (New) The composition of claim 119 wherein the mesenchymal stem cells are autologous to the donor.

122. (New) The composition of claim 119 wherein the mesenchymal stem cells are allogeneic to both the recipient and the donor.

123. (New) The composition of claim 119 wherein said mesenchymal stem cells are human mesenchymal stem cells.

124. (New) The composition of claim 119 wherein the mesenchymal stem cells are xenogeneic to both the recipient and the donor.

125. (New) The composition of claim 119 wherein said mesenchymal stem cells have been expanded in culture.

126. (New) A composition for reducing an adverse immune response against a graft recipient caused by a graft, comprising a member selected from the group consisting of mesenchymal stem cells and a supernatant from a mesenchymal stem cell culture in an amount effective to reduce the adverse immune response against the graft recipient caused by the graft, and a pharmaceutical carrier.

127. (New) The composition of claim 126 wherein the mesenchymal stem cells are autologous to the recipient.

128. (New) The composition of claim 126 wherein the mesenchymal stem cells are autologous to the donor.

129. (New) The composition of claim 126 wherein the mesenchymal stem cells are allogeneic to both the recipient and the donor.

130. (New) The composition of claim 126 wherein the mesenchymal stem cells are xenogeneic to both the recipient and the donor.

131 123. (New) The composition of claim 119 wherein said mesenchymal stem cells are human mesenchymal stem cells.

132 125. (New) The composition of claim 119 wherein said mesenchymal stem cells have been expanded in culture.

133 126. (New) A process for reducing in a transplant recipient an immune response of effector cells against an alloantigen to the effector cells, comprising transplanting to the transplant recipient a transplant contacted, prior to transplantation, with tissue obtained from the transplant recipient and then contacted with a member selected from the group consisting of mesenchymal stem cells and a supernatant of a mesenchymal stem cell culture in an amount effective to reduce an immune response against the recipient by the donor transplant.

134 127. (New) The process of claim 126, wherein the effector cells are T cells.

135 128. (New) The process of claim 127, wherein the T cells are from the donor and the alloantigen is from the recipient.

136 129. (New) The process of claim 127, wherein the T cells are from the recipient and the alloantigen is from the donor.

130. (New) The process of claim 126, wherein the mesenchymal stem cells are human mesenchymal stem cells.

131. (New) The process of claim 126, wherein the mesenchymal stem cells are xenogeneic mesenchymal stem cells.

132. (New) The process of claim 126 wherein the donor transplant is bone marrow.

133. (New) The process of Claim 126 wherein the donor transplant is peripheral blood.

134. (New) The process of claim 126, further comprising administering to the recipient immunosuppressive agents.

REMARKS

The present application is a divisional of Application Serial No. 09/427,333, filed 26 October 1999, and the first paragraph of the specification has been amended to reflect this fact. Otherwise, the submitted application is a true copy of the parent case and no new matter has been added. In addition, because claims have been allowed in the two parent applications, the claim set has been amended to reflect claims to embodiments not believed covered by the allowed claims of the parent applications.

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Commissioner for Patents
Washington, DC 20231

Alan J. Grant 11/13/01

Alan J. Grant, Esq. **Date**

Respectfully submitted,

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